

Claims 1-66 (cancelled).

67. (new) A method for producing a polypeptide product which is substantially free of a specific undesired protein that hinders the use of the polypeptide product, wherein the undesired protein has activity that is essential for survival of a host cell or for a viable production process using a host cell, the method comprising

(a) identifying a mutant form of said polypeptide product which has increased tolerance to a particular reaction condition selected from pH or temperature, than a corresponding wild-type polypeptide product,

(b) identifying a mutant form of said undesired protein which has decreased tolerance to said reaction condition than a wild-type form of said undesired protein, and is denatured under conditions at which the mutant form of the polypeptide product identified in step (a) is stable,

(c) transforming a host cell so that it expresses the mutant form of the polypeptide product identified in step (a),

(d) further transforming the host cell so that it expresses the undesired protein only in the mutant form identified in step (b),

(e) culturing said host cell and recovering the desired product, wherein either the host cell culture or the recovered product is subjected for a sufficient period of time to conditions at which the undesired protein is denatured but the polypeptide product remains unaffected.

68. (new) A method for producing a polypeptide product which is substantially free of a specific undesired protein that hinders the use of the polypeptide product, wherein the undesired protein has activity that is essential for survival of a host cell or for a viable production process using a host cell, the method comprising

(a) identifying a mutant form of said polypeptide product which has increased thermostability than a corresponding wild-type polypeptide product,

(b) identifying a mutant form of said undesired protein which has decreased thermostability than a wild-type form of said undesired protein, and is denatured under conditions at which the mutant form of the polypeptide product identified in step (a) is stable,

(c) transforming a host cell so that it expresses the mutant form of the polypeptide product identified in step (a),

(d) further transforming the host cell so that it expresses the undesired protein only in the mutant form identified in step (b),

(e) culturing said host cell and recovering the desired product, wherein either the host cell culture or the recovered product is subjected for a sufficient period of time to a temperature at which the undesired protein is denatured but the polypeptide product remains unaffected.

69. (new) A method according to claim 67 or claim 68 wherein the step (a) is carried out by mutating colonies of host cells using non-specific methods, differentially screening colonies that are able to grow at 25°C but not able to grow at 37°C, and screening these colonies for activity of the specific undesired protein at various temperatures.

70. (new) A method according to claim 67 or claim 68 wherein in step (d) a host cell is transformed so that chromosomal genes expressing the said undesired protein are inactivated, and a gene which expresses the mutant form of the protein identified in step (b) is introduced into the host cell on a plasmid.

71. (new) A method according to claim 68 wherein the temperature used in step (e) is 37°C.

72. (new) A method according to claim 67 or claim 68 wherein the polypeptide product is a luciferase, and the specific undesired protein is adenylate kinase.

73. (new) A method for producing a polypeptide product which is substantially free of a specific undesired cellular protein that hinders the use of the polypeptide product, wherein the undesired protein has activity that is essential for survival of a host cell or for a viable production process using the host cell, the method comprising

culturing a host cell which has been transformed so that it expresses said polypeptide product and further transformed so that it expresses said undesired protein only in a mutant form which form has the said activity of the corresponding native protein under culture conditions but is denatured under conditions at which the said polypeptide product remains unaffected; and recovering the desired product, wherein either the host cell culture or the recovered product is subjected for a sufficient period of time to conditions under which the undesired protein is denatured but the polypeptide product remains unaffected.

74. (new) A method according to claim 73 wherein the host cells are cultured for a period which is sufficient to allow production of polypeptide product, and then a batch of said culture is subjected to the said conditions under which the undesired protein is denatured, and the polypeptide product is recovered from the said batch.

75. (new) A method according to claim 73 wherein the conditions at which the undesired protein is denatured and the polypeptide product remains unaffected are a predetermined temperature or pH conditions.

76. (new) A method according to claim 75 wherein the conditions at which the undesired protein is denatured and the polypeptide product remains unaffected are a predetermined temperature.

77. (new) A method according to claim 76 wherein the predetermined temperature is 37°C.

78. (new) A method according to claim 77 wherein the host cell or the recovered product is subjected to a temperature of from 37°C, up to the temperature at which the desired polypeptide product is denatured.

79. (new) A method according to claim 73 wherein the conditions at which the undesired protein is denatured and the polypeptide product remains unaffected are pH conditions.

80. (new) A method according to claim 73 wherein the desired polypeptide product is luciferase and the undesired protein is adenylate kinase.

81. (new) A method according to claim 80 wherein the adenylate kinase is thermolabile at a temperature of 37°C.

82. (new) A method according to claim 81 wherein the adenylate kinase includes mutations at amino acids 87 or 107 in the sequence of E. coli adenylate kinase.

83. (new) A recombinant cell which has been transformed so that it expresses a first nucleotide sequence which encodes a desired polypeptide under the control of regulatory elements which allow expression of said polypeptide, and is further transformed so that it expresses a specific protein which is undesirable as a contaminant in preparations of said polypeptide product but wherein the undesired protein has activity that is essential for survival of a host cell or for a viable production process using the host cell, only in mutated form such that the protein expressed is denatured under conditions in which the polypeptide product remains unaffected.

84. (new) A recombinant cell according to claim 83 wherein the said desired polypeptide comprises a luciferase and the said undesired protein comprises adenylate kinase.

85. (new) A recombinant cell according to claim 83 which further comprises at least one selection marker.

86. (new) A recombinant cell according to claim 83, which comprises a prokaryotic cell.

87. (new) A recombinant cell according to claim 83 which comprises a recombinant *E. coli* cell.

88. (new) A method for producing a recombinant cell according to claim 83 which method comprises in any order (a) transforming a host cell with a vector which encodes said undesired protein in a form which is denatured under given conditions, subjecting transformants to said conditions and detecting those in which protein product is denatured, and (b) transforming said host cell with a vector which encodes a desired polypeptide which is unaffected under said conditions and a first selection marker, and using the first selection marker to detect stable transformants.

89. (new) A method according to claim 88 wherein the vector which encodes said undesired protein in a form which is denatured under given conditions further comprises a second selection marker which is different to said first selection marker, and stable transformants are selected.

90. (new) A method according to claim 89 wherein said selection markers comprise particular different antibiotic resistance genes.

91. (new) A method for producing a polypeptide product which is substantially free of a specific undesired protein that hinders the activity of the polypeptide product, wherein the undesired protein has activity that is essential for survival of a host cell or for a viable production process using the host cell, the method comprising culturing a host

cell which has been transformed so that it expresses said polypeptide product and further transformed so that it expresses said undesired protein only in a mutant form which form has the said activity of the corresponding native protein under culture conditions but is denatured at temperatures at which the said polypeptide product remains unaffected; and

recovering the desired product, wherein either the host cell culture or the recovered product is subjected for a sufficient period of time to a temperature at which the undesired protein is denatured but the polypeptide product remains unaffected.

92. (new) A method according to claim 91 wherein the host cells are cultured for a period which is sufficient to allow production of polypeptide product, and then a batch of said culture is subjected to said conditions of temperature under which the undesired protein is denatured, and the polypeptide product is recovered.

93. (new) A method according to claim 91 wherein the temperature is 37°C.

94. (new) A method according to claim 91 wherein the host cell or the recovered product is subjected to a temperature of from 37°C, up to the temperature at which the desired polypeptide product is denatured.

95. (new) A method according to claim 91 wherein the desired polypeptide product is luciferase and the undesired protein is adenylate kinase.



96. (new) A method according to claim 95 wherein the adenylate kinase is thermolabile at a temperature of 37°C.

97. (new) A method according to claim 96 wherein the adenylate kinase includes mutations at amino acids 87 or 107 in the sequence of E. coli adenylate kinase.

98. (new) A recombinant cell which has been transformed so that it expresses a first nucleotide sequence that encodes a desired polypeptide under the control of regulatory elements which allow expression of said polypeptide, and is further transformed so that it expresses a specific undesired protein that hinders the use of the polypeptide product but has activity that is essential for survival of a host cell or for a viable production process using the host cell, only in mutated form such that the protein expressed is denatured at a temperature at which the polypeptide product remains unaffected.

99. (new) A recombinant cell according to claim 98 wherein the said desired polypeptide comprises a luciferase and the said undesired protein comprises adenylate kinase.

100. (new) A recombinant cell according to claim 98, which further comprises at least one selection marker.

101. (new) A recombinant cell according to claim 98, which comprises a prokaryotic cell.

102. (new) A recombinant cell according to claim 98 which comprises a recombinant E. coli cell.

103. (new) A method for producing a recombinant cell according to claim 98 which method comprises in any order (a) transforming a host cell with a vector which encodes said undesired protein in a form which is denatured under given temperature conditions, subjecting transformants to said temperature conditions and selecting those in which protein product is denatured, and (b) transforming said host cell with a vector which encodes a desired polypeptide which is unaffected under said temperature conditions and a first selection marker, and using the first selection marker to detect stable transformants.

104. (new) A method according to claim 103 wherein the vector which encodes said undesired protein in a form which is denatured under given temperature conditions

further comprises a second selection marker which is different to said first selection marker, and stable transformants are selected.

105. (new) A method according to claim 104 wherein said selection markers comprise particular different antibiotic resistance genes.

106. (new) A method for producing a luciferase which is substantially free of adenylate kinase, the method comprising culturing a host cell which has been transformed so that it expresses a luciferase which is thermostable at 37°C, and expresses adenylate kinase only in a mutant form which form is denatured at temperatures of 37°C; and recovering the luciferase, wherein either the host cell culture or the recovered luciferase is subjected for a sufficient period of time to temperatures at which the adenylate kinase is denatured but the luciferase remains unaffected.